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APPLICATION NUMBER: *60/544,459*
FILING DATE: *February 12, 2004*

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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[X] *Additional inventors are being named on the 1 separately numbered sheets attached hereto.*

TITLE OF THE INVENTION (280 characters max)

METHOD AND SYSTEM FOR ACOUSTIC EMBOLI DIVERSION IN THE AORTIC ARCH

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[X] Applicant claims small entity status. See 37 CFR 1.27.

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

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Respectfully submitted,

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Date February 12, 2004

REGISTRATION NO. (*if appropriate*) 24,156

Docket Number: 206,448

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

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Docket Number	206,448	Type a plus sign (+) inside this box →	+

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Number 2 of 2

Method and system for acoustic emboli diversion in the aortic arch

Background

Intra-operative cerebral embolism is considered as one of the major sources of mortality and morbidity following cardiac surgery, resulting in neurological impairment of the patient. The current incidence of neurological impairment following cardiac surgery is estimated as 3% of stroke and more than 40% of permanent cognitive deficit.

Methods and devices for elimination of cerebral emboli inside the human body via their diversion or blocking by acoustic forces and avoiding their passage to the brain has been described by MILO in a PCT application No. PCT/IB00/01785 and U.S. patent application 10/162,824, whose disclosures are incorporated herein by reference. The PCT application cited above teaches of various embodiments for diversion of intra-corporeal emboli using a variety of methods, such as

- "Collar" mounted around the neck of the patients, containing transducers pointing at the carotid bifurcation or the great origins on the aortic arch.
- Transducer means coupled to the ascending aorta of the patient whose acoustic beam diverts emboli.
- Transducers, introduced into the esophagus or the trachea of the patient, pointing toward the heart and the ascending aorta, such as to divert emboli towards preferred locations.

Summary of the invention

In summary, the concept of non-invasive acoustic diversion of emboli flowing in the aortic arch so as to avoid their passage into the great origins of the neck vessels is very attractive from the standpoint of elimination of cerebral embolism during cardiac surgery. It would be desirable to position a transducer used for this purpose very close to the aortic arch, but still outside of the region where most of the surgical activity takes place, i.e. away from the heart and the ascending aorta. It is also desirable to avoid the perforation of the aorta, as described in some of the embodiments in the above-mentioned PCT and U.S. patent applications.
The present patent application describes a method and a device for the diversion and/or blocking of emboli (air or thrombi originating inside the heart or fragments of atheromateous plaque detached from the aortic valve or the ascending aorta due to surgical maneuvers), flowing in the aortic arch in order to avoid their passage through the great origins of the vessels leading to the brain (innominate artery and left common carotid artery), during a procedure of cardiac surgery. In embodiments of the invention, an ultrasonic transducer or transducers for this purpose are placed within the patient's chest cavity, in a location that is not directly adjacent to the heart or aortic arch, and are aimed toward the aorta so as to divert emboli toward the descending aorta and away from the vessels leading to the brain.

The unique features of the present invention are:

1. The transducer or transducers are positioned in proximity to the great origins of the neck vessels in the aortic arch, thus significantly simplifying the problem of

alignment and of the transducers and requiring less acoustic power to be generated

2. The transducer or transducers are positioned in a location which does not interfere with standard surgical protocols or other devices which are positioned near the heart or the ascending aorta
3. The aorta is not required to be perforated by any vent needle
4. Simple stabilization of the transducers in place by virtue of the unique thoracic anatomy following standard Median Sternotomy incision
5. Dedicated acoustic operating regime which minimizes the energy imparted to the body of the patient, thus reducing safety problems

Description of the invention

The invention is based on the specific anatomy of the chest incision in cardiac surgery. In standard cardiac surgery the chest bone (sternum) is fully cut up to the sternal notch (base of neck). The two parts of the sewed sternum are then spread using a retractor device in order to allow the surgeon access to the heart and the ascending aorta. This type of incision, which is coined Median Sternotomy, being the most common incision in cardiac surgery, is depicted in Figure 1 below.

Figure 1 depicts a typical chest cavity created when both parts of the sternum are spread using a retractor and the pericardium is opened to expose the heart and part of the ascending aorta and the vena cava. All the parts above the exposed heart and ascending aorta, such as the aortic arch, the great origins, the Innominate Vein etc are shown in Figure 1 using dashed line, for clarity. These parts are not exposed in the surgical procedure and remain covered by the pericardium or a couple of millimeters of connective tissue. Figure 1 also depicts the "Free Space Zone" (FSZ), which is the upper part of the chest cavity (i.e. that part which is most proximal to the head). On one hand, the FSZ resides externally to the region where most of the surgical activity takes place (i.e. the heart and the ascending aorta), but on the other hand the FSZ is located in very close proximity to the great origins of the neck vessels on the aortic arch where only a couple of millimeters of tissue separate them. It should be noted that part of the FSZ is exposed by the surgical incision (i.e. the part close to the heart, cf. Figure 1) while other part of the FSZ (i.e. close to the head) is actually hidden below the skin close to the upper part of the incision, in the form of a cavity (better seen in Figure 2 below).

Figure 2 below depicts a schematic drawing of a side-view cross section of the chest cavity including the heart, the aorta, the vena cava and the great origins of the neck vessels. The FSZ is clearly seen as a well-defined cavity surrounded be tissue with only one opening and a layer of skin serving as the "ceiling" of this cavity.

The location of the FSZ in very close proximity to the great origins of the neck vessels on the aortic arch as well as the fact that this site is not being exploited for surgical maneuvers or devices, make it a perfect candidate for positioning of power transducer/s whose acoustic beam is oriented towards the aortic arch in order to divert or block emboli flowing in the ascending aorta and aortic arch and avoiding their passage into the great origins of the neck vessels.

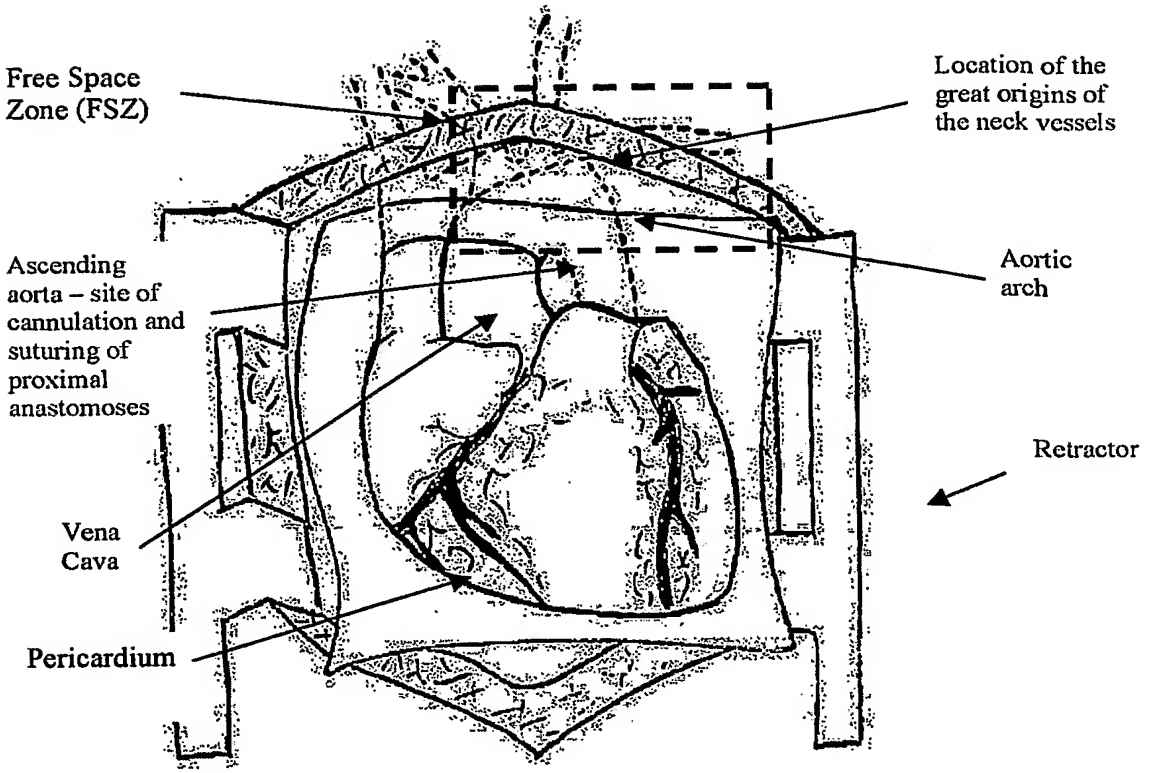

Figure 1 – General sketch of the chest cavity in a Median Sternotomy incision

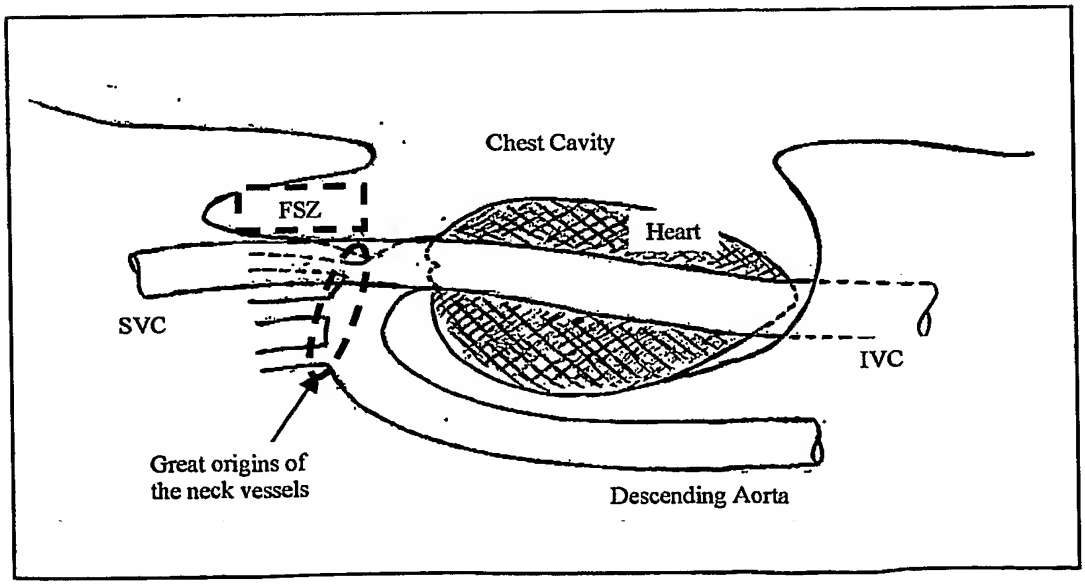

Figure 2 - side-view cross section of the chest cavity in Median Sternotomy incision

Figure 3 below depicts a power transducer, which is located in the FSZ with its acoustic beam aligned towards the aortic arch in an angle of orientation in between the direction of the average blood flow in the aortic arch and the average blood flow in the neck vessels branching off at the aortic arch. Figure 3 also depicts a typical trajectory of an embolus emanated from the heart, the aortic valve or the walls of the ascending aorta (which are the locations from which the vast majority of the autologous emboli originate). Upon flowing in the ascending aorta towards the aortic arch, the embolus enters the acoustic beam generated by the power transducer. The embolus is then deflected away from the great origins of the neck vessels by virtue of the acoustic force exerted on it along the direction of propagation of the acoustic wave.

Although Figure 3 depicts a specific orientation of the acoustic beam, it is clear that there are also other orientations of the acoustic beam, which will block the passage of emboli into the neck vessels. Thus, any orientation of the acoustic beam for the purpose of deflecting embolic flow away from the great origins is to be considered as covered by the present invention.

It should also be noted that same effect may be achieved with more than one transducer, if necessary. Thus, singular language clearly does not limit the scope of this invention and using multiple transducers, also falls within the scope of this invention.

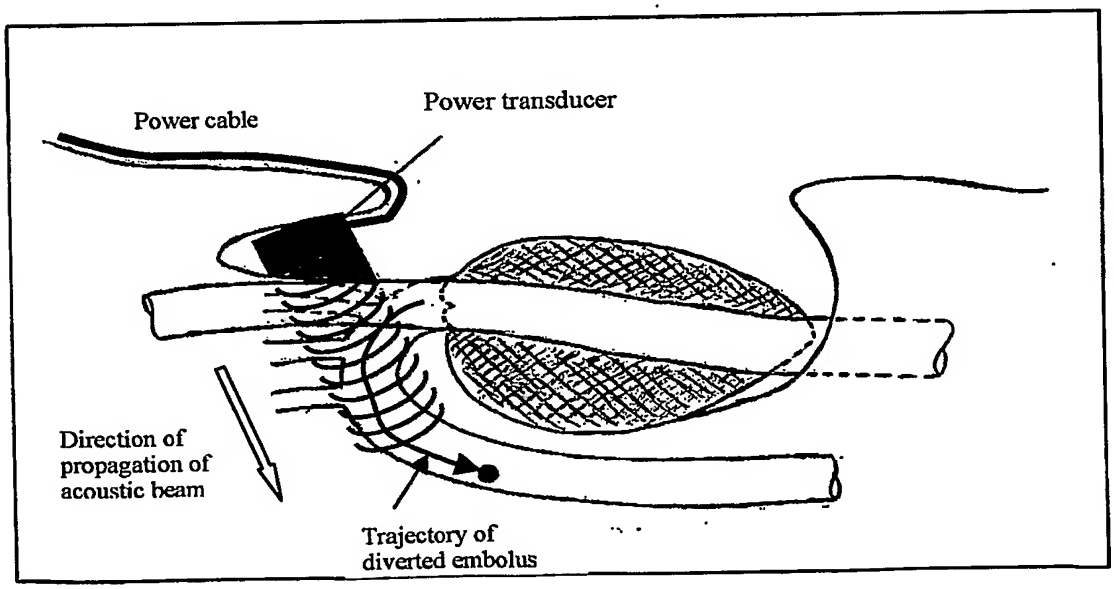

Figure 3 – Position of the power transducer in the FSZ and diverting emboli

Positioning and stabilization of transducer within the FSZ

The positioning and stabilization of the transducer within the FSZ can be done in a variety of methods:

- Vacuum coupling
  The transducer is coupled to a matching layer shaped so as to create a closed hollow cavity when positioned on the surface of the tissue covering the aortic arch and the great origins (usually, a connective tissue), see the left picture in Figure 4 below. The matching layer possesses acoustic properties close to those of soft tissue, e.g., made from Latex, Polyurethane, Polyethylene or similar material. A pipe drilled through the transducer connects the cavity and an external vacuum pump.
  Once vacuum is pulled through the pipe, the hollow cavity is closed and full contact established between the matching layer and the surface of the tissue, see the right picture in Figure 4 below. The external pressure holds the transducer and matching layer firmly in place. The transducer can be easily detached once air is allowed to enter the pipe. Clearly, a very low vacuum level of 0.9 Bar or less is sufficient for the above purpose.

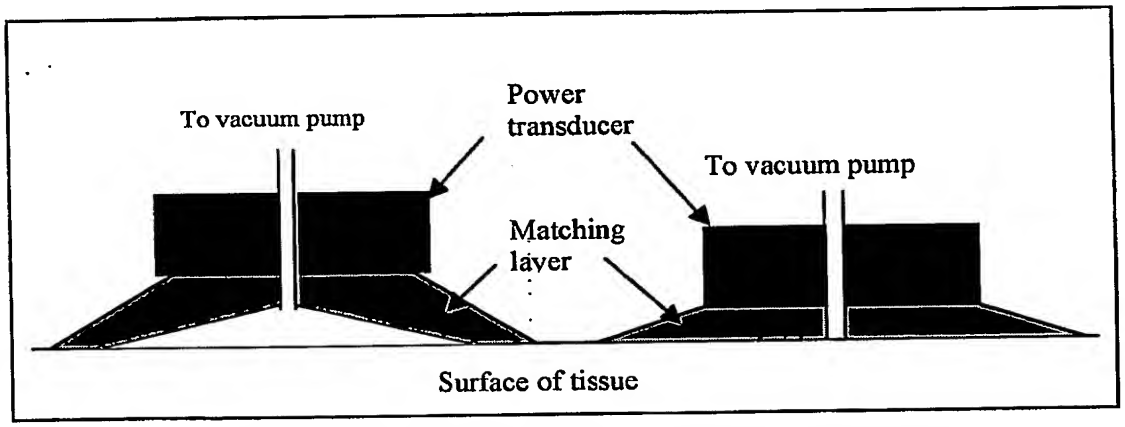

Figure 4 – Vacuum based transducer coupling and stabilization

- Liquid bag
  The transducer is encapsulated within a flexible bag made from any type of polymer such as but not limited to Latex, Polyethylene and Polyurethane. The liquid bag is connected to a liquid pump through two ports which pumps liquid at a controlled temperature (preferably cooled) into and out from the liquid bag. Once the bag is filled with liquid, it expands, fills the volume of the FSZ and presses the transducer and matching layer against the surface of the tissue, thus achieving three purposes: 1) Stabilization of the transducer 2) Acoustic coupling to the tissue below, and 3) Removal of heat generated within the transducer and cooling of the tissue below. The situation is depicted in Figure 5 below:

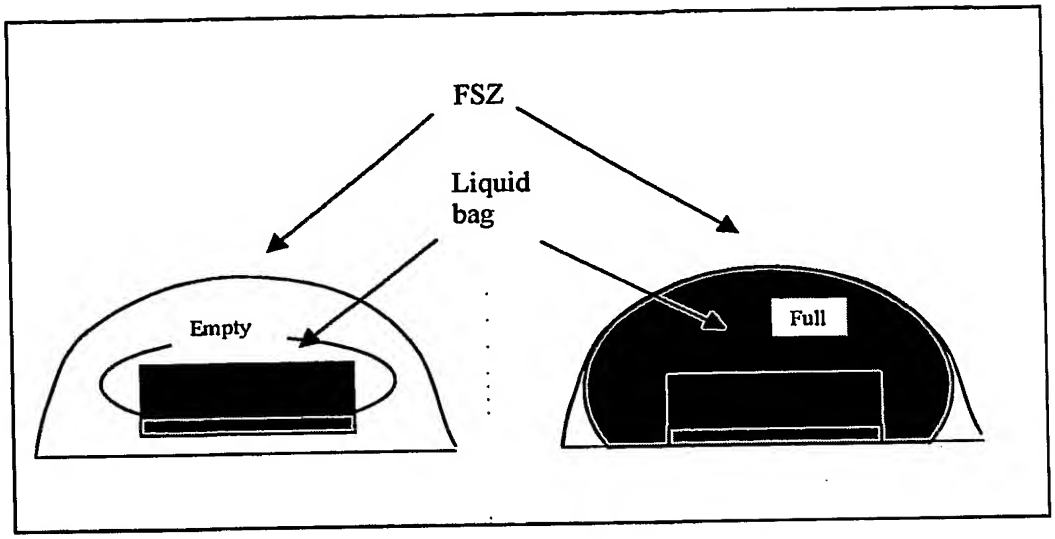

Figure 5 – Concept of liquid bag transducer coupling and stabilization

- Fastening to the retractor
  Once opened, thus spreading the two parts of the sawed sternal bone, the retractor constitutes a rigid structure on which the transducer can be mounted to ensure stability and minimize its movement relative to the body of the patient during surgical procedure.

- Sewing to proximal tissue
  Sewing of surgical devices to tissue such as skin, muscle etc is a very common fixation and stabilization technique in cardiac surgery. This method will require a few loopholes on the transducer, through which sewing to adjacent tissue will be done. Approximately 3-4 such sutures will be sufficient to fix transducer in place.

Any combination of the positioning and stabilization methods described above, e.g. sewing to proximal tissue and expandable liquid bag is to be considered as covered by the present invention.

Methods of transducer alignment

The embolic flow within the ascending aorta and the aortic arch can best be controlled so as to avoid its passage into the neck vessels if the acoustic beam, generated by the power transducer, impinges on the great origins and their vicinity. Thus, the power transducer has to be aligned (i.e. appropriate position and orientation of the transducer). Below disclosed are two possible methods of transducer alignment:

- Focused ultrasonic beam
  Each power transducer generates a relatively focused ultrasonic beam, i.e. with a beam diameter in the range of 5-30 mm. The transducer should be aligned so that the beam will point toward specific locations on the aortic arch such as the ostia (the orifices) of the neck vessels or slightly upstream so as to result in effective

emboli diversion. The advantages of this method is that only a small part of the aorta is exposed to ultrasonic energy and a small ultrasonic power is imparted into the body of the patient. The disadvantage is that this method requires a precise alignment of the transducer such that the narrow beam impinges on the correct position of the aorta. For that purpose an auxiliary guiding mechanism can be used, e.g. a Doppler transducer diagnostic transducer which will be integrated concentrically within the power transducer, to create a hybrid transducer, and will provide correct alignment data (cf. Figure 6 below). The correct positioning of the hybrid transducer will be based on a detection of the Doppler signature from the orifice of a great origin. When maximal Doppler signals are obtained, it ensures that the power ultrasound beam correctly covers the origin.
The Doppler acoustic technology is well known and accepted in medical imaging to detect blood vessels and measure blood velocity In-Vivo.
It should be noted that combinations of a Doppler transducer and a power transducer, other than concentric can be designed by an average person skilled in the art. Such combinations should be considered as covered by the present invention.

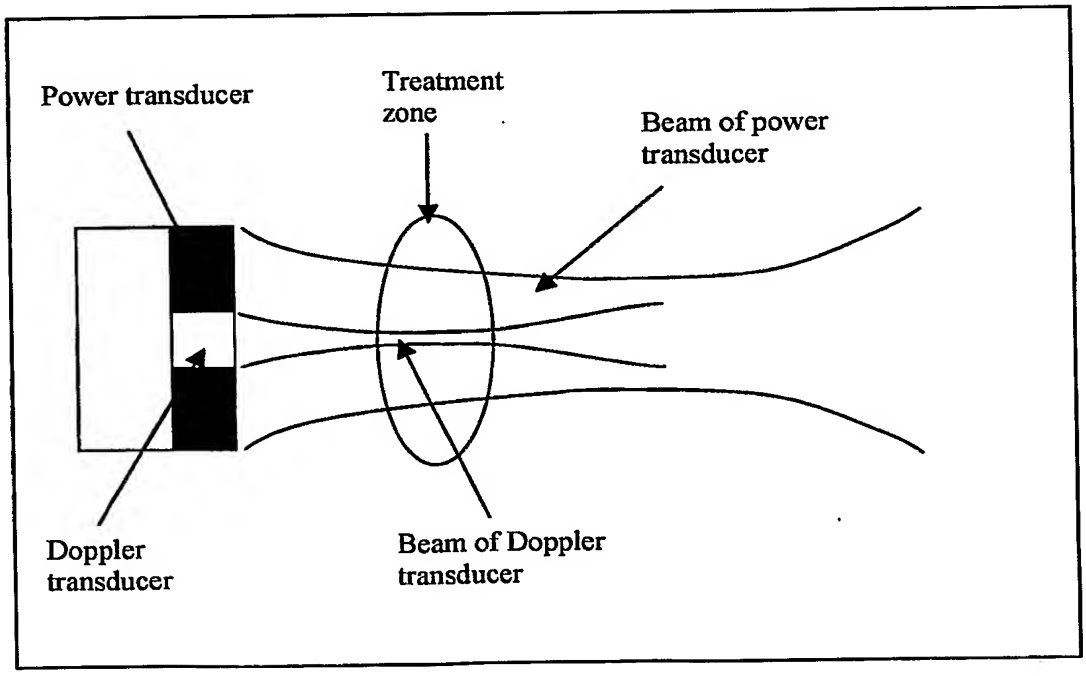

Figure 6 – A sketch of a Doppler transducer integrated within the power transducer

- Unfocused ultrasonic beam
  In this concept the power transducer emits a wide acoustic beam, wide enough to cover the great origins of the neck vessels on the aortic arch without having to utilize a specific alignment mechanism. This means that the surgeon will position

the transducer in the FSZ based on his knowledge of the anatomy of the aortic arch and the relative locations of the great vessels. The acoustic beam will be wide enough to cover the great origins and compensate for inaccuracy of the positioning of the transducer by the surgeon and natural variations in anatomy between different subjects.
The drawback of the wide-beam is the need to generate much more acoustic power which will be imparted to body regions adjacent to the great origins and may cause thermal heating of the tissue.

Transducer activation regime
The power transducer may be activated in several possible regimes

- Continuous activation in fixed power through whole operation period
  In this activation regime the transducer is continuously operated during the whole period of its deployment within the chest cavity. In this case it has to be operated at a relatively high power so as to enable diversion of fast emboli flowing in the aorta during the peak systole where their velocity is maximal (this statement is relevant to cases where the heart is beating or on a heart-lung machine operating in pulsatile mode). Although, this is the most simple activation method, it is inefficient from the energetic standpoint and may cause excessive heating of the patient tissue

- Continuous activation in synchronization with the cardiac output
  In this activation regime the transducer is continuously operated within the chest cavity during the whole period of its deployment within the chest cavity. However, the instantaneous power of the transducer is not constant but rather oscillating in synchronization with the cardiac output which correlates well with the blood flow velocity (the latter is approximately equal to the flow velocity of the emboli). This way, high acoustic power is generated during peak systolic velocity (when emboli flow fast) and low power is generated during diastolic or retrograde flow, when emboli move slowly and do not require high acoustic intensity to be diverted. This method allows efficient diversion with average acoustic power which corresponds to the average velocity of emboli in the circulation which is around 3-4 times lower than the peak systolic velocity. Thus this method, reduces potential tissue heating by 3-4 fold compared with the method above (continuous activation in fixed power).
  This method is relevant only when the patient is off the heart-lung machine or when the heart-lung machine is operated in pulsatile mode. The synchronization between the transducer and the cardiac output can be accomplished via data recorded by standard ECG devices, intra-vascular blood pressure monitors or oxygen saturation monitoring devices. (All these devices are commercially available and provide real-time output data, which may be used as an input to synchronize the power ultrasound)

- Intermittent activation
  This activation regime is based on the fact that most emboli originating within the body (heart, aortic valve and ascending aorta) are not released into the circulation spontaneously but rather in conjunction with specific surgical maneuvers, such as cannulation, de-cannulation, de-clamping, re-activation of the heart etc. In this

operation regime, the activation of the transducer is to be done by the surgeon shortly prior to performing one of the above surgical maneuvers, for a short period of time up to several minutes. This method is the most efficient from the energetic and tissue-heating standpoints, because the system is idle most of the time, however it will not enable diversion of emboli that are released during periods other than in conjunction with the above maneuvers. Note that, in this mode of intermittent activation, the activation of the transducer can be done both in continuous mode and fluctuating in synchronization with the cardiac output

Ex-Vivo experiments

The effect of diversion of embolic flow in the aortic arch by power ultrasound was experimentally investigated Ex-Vivo on an aortic model made of latex (as a tissue mimicking material). The experimental setup is given in the following Figure

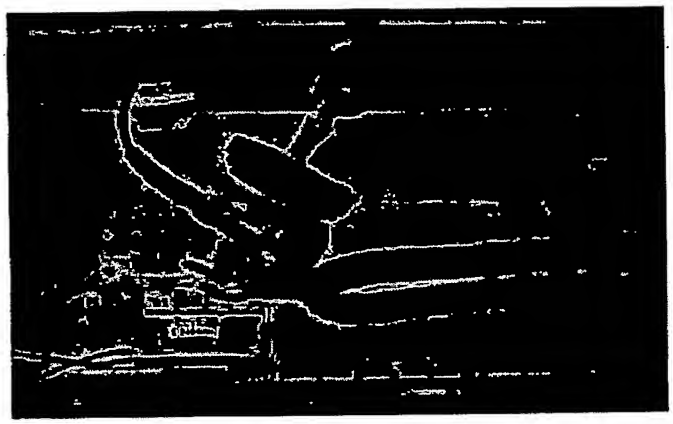

Figure 7 – Ex-Vivo experimental setup

Figure 7 above shows the synthetic latex model of the aorta with a single bifurcation (mimicking the Innominate Artery) protruding at the aortic arch and connected down stream to a transparent pipe such that the particles flowing through the bifurcating vessel may be visually observed. The transducer is seen connected to a holding arm with its acoustic beam oriented towards the origin of the bifurcating vessel.
The flow in the aorta was kept in closed circuit, filled with a suspension of polyethylene grains with sizes of 500-750 micron, simulating the emboli, in water.

The acoustic parameters used in this experiment were:

- Transducer diameter – 38 mm
- Frequency – 2.25 MHz
- Electrical power – 10-20 Watt
- Average flow velocity – 30 cm/sec

Figure 8 below shows pictures of the embolic flow in the bifurcated vessel (in its transparent segment) when the power ultrasound is ON (right picture) compared with a control experiment (power ultrasound OFF). The dramatic decrease in the embolic

flow through the bifurcated vessels by virtue of the power ultrasound is very clearly seen in Figure 8.

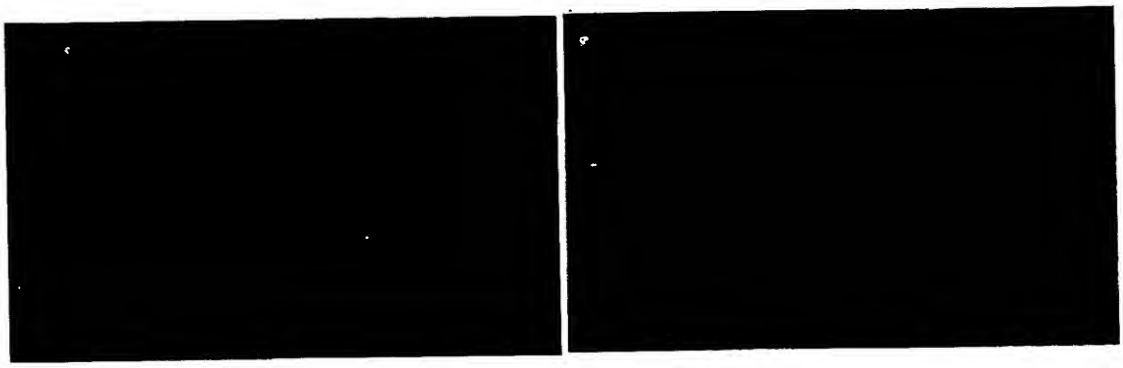

Figure 8 – Pictures of embolic flow in the bifurcating vessels in the absence of power ultrasound (control experiment, left picture) and with power ultrasound ON (right picture)

Animal feasibility study

The method and device disclosed in this application has also been investigated in an animal feasibility study. In this study, the chest of a domestic pig, weighing 70 kg, was opened using Mid Sternotomy technique, such that the heart, aorta and Innominate Artery were exposed.

After exposure of the aortic arch the power transducer (same transducer used in the Ex-Vivo experiments) was positioned such that its beam was pointed on a point on the aortic arch slightly upstream of the bifurcation of the Innominate Artery. A diagnostic probe (Linear probe 10LB connected to a commercial GE LogiQ Book ultrasonic imaging system) was positioned upstream on the Right Common Carotid Artery (RCCA) in order to monitor the embolic flow into the animal's head. The positioning of the power transducer and the diagnostic probe situation is schematically depicted in Figure 10 and its picture is given in Figure 11 below:

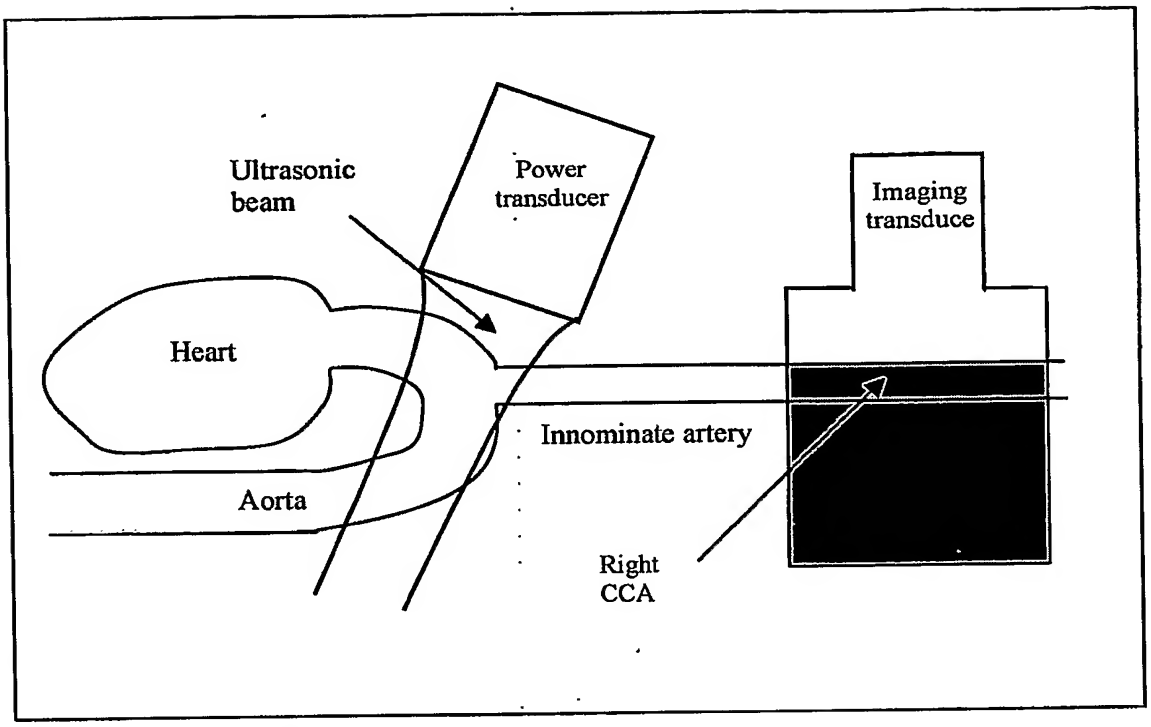

Figure 10 – Schematic view of transducers positioning

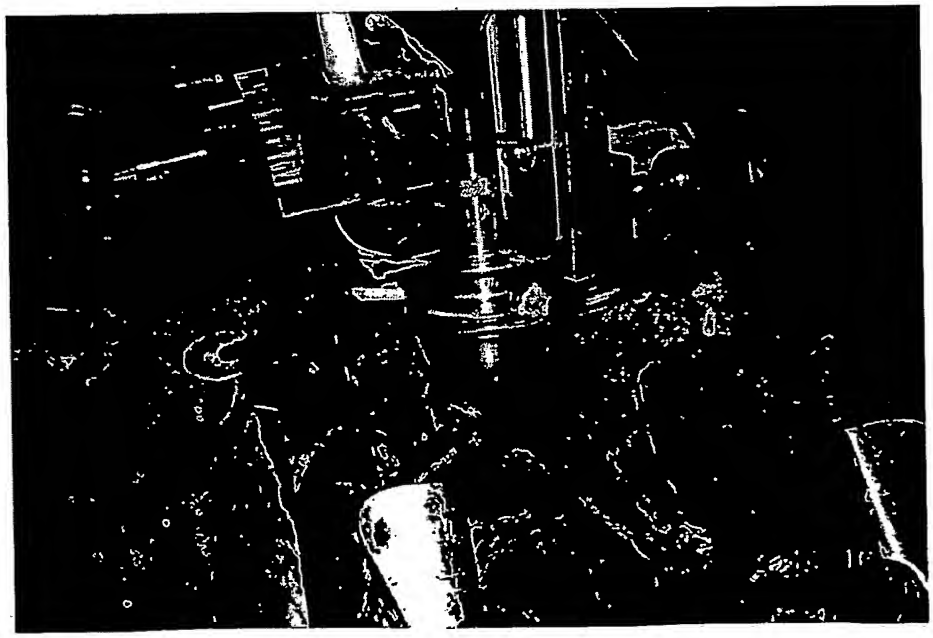

Figure 11 – Photo of the exposed heart, power transducer and diagnostic probe positioned in place

In order to simulate flow of embolic material originating from the heart and the ascending aorta, two types of embolic materials were used in this experiment

- Gaseous emboli – 8 cc of air
- Solid emboli – 800 polystyrene microspheres suspended in 10cc of saline

The embolic material was injected directly into the left ventricle of the beating heart and then fully pumped by the heart into the aorta in the next few heart beats.

The efficacy of the diversion of the embolic material and consequently its blocking from entering the Innominate Artery was visually demonstrated by continuous monitoring and imaging of the animal's Right Common Carotid Artery (RCCA). In order to generate a single arterial flowing path from the Innominate Artery to the RCCA, where the emboli were monitored, the Right Subclavian Artery and the Left Common Carotid Artery were clamped (these branch from the Innominate Artery). Therefore, every embolus flowing into the Innominate Artery was "forced" to flow through the RCCA, where it was ultrasonically visualized.

The measured parameter was the number of emboli flowing through the RCCA, using cine-loop video clips, generated by the diagnostic ultrasound, in which every embolus is clearly seen. The efficacy of the system was determined by comparing the number of emboli flowing in the RCCA when the power transducer was ON to the same measured figure when the power transducer was OFF (keeping a controlled and constant quantity of embolic material injected into the left ventricle).
In this experiment described above, it has been demonstrated that the activation of power ultrasound, yields a 90-95% reduction in number of emboli flowing through the RCCA

Figure 12 below presents two pictures acquired by the LogiQ Book ultrasonic system, providing a typical demonstration of the embolic flow through the RCCA when the power ultrasound is ON (right picture) compared with the control experiment (left picture). The dramatic decrease in the embolic flow through the RCCA by virtue of the power ultrasound is clearly seen in Figure 12.

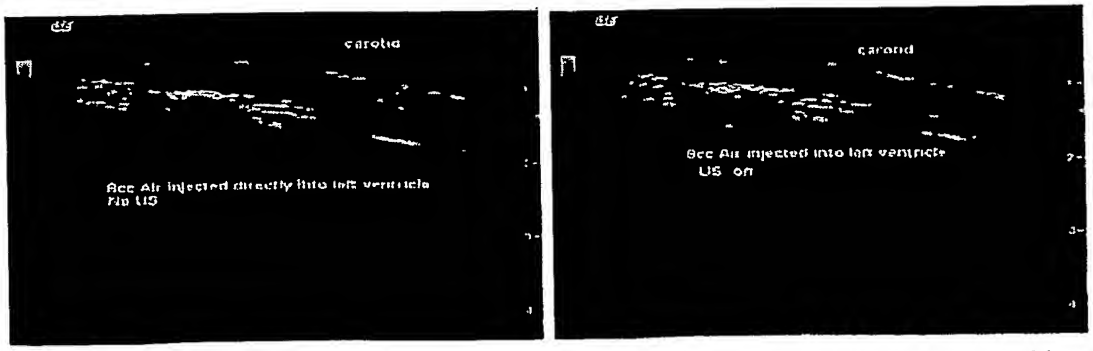

Figure 12 – Left picture shows "shower" of air bubbles flowing through the carotid artery in the control experiment (the lumen if full of gray spots). The right picture shows the carotid artery clean of bubbles while the power ultrasound is ON (cf. the black color of the lumen)